THE ACTION OF SNAKE VENOM UPON COLD-BLOODED ANIMALS.

By HIDEYO NOGUCHI, M. D.,
Assistant in Pathology, University of Pennsylvania.

Washington, U. S. A.:
Published by the Carnegie Institution,
June, 1904.

Carnegie Institution of Washington,
Publication No. 12.

3389

Press of Gibson Bros.,
Washington, D. C.

THE ACTION OF SNAKE VENOM UPON COLD-BLOODED ANIMALS.

By HIDEYO NOGUCHI, M. D.,
Assistant in Pathology, University of Pennsylvania.

Since the writings of Fontana, Weir Mitchell alone seems to have concerned himself with the study of the action of snake venom upon cold-blooded animals. Having studied and described the action of rattlesnake venom upon frogs and upon *Crotalus* itself, it was his intention, as will appear from a paragraph in his earlier paper on venom, to extend his observations to a wider class of animals. Thus he writes:

"It was my intention to examine, in the next place, the effects of the venom upon leeches, fish, eels, and crustacean animals, but for some reasons, which it is needless to relate, I was obliged to postpone these observations until some future occasion."*

The present investigation is the outcome of Dr. Mitchell's interest in this subject, and has been rendered easily possible by the facilities of the Marine Biological Laboratory at Woods Hole, Massachusetts, and by the aid of a grant from the Carnegie Institution of Washington. I wish to thank Dr. Mitchell for arousing my interest in this subject and for many suggestions as to the manner of its pursuit. I am also under obligations to Prof. C. O. Whitman for placing at my disposal the materials for carrying on the study.

The following orders of animals were tested against venom: Reptilia, Amphibia, Pisces, Insecta, Crustacea, Vermes, Mollusca, Echinodermata.

Several kinds of venom were employed: cobra, water moccasin, and rattlesnake. All had been previously dried, and hence they were dissolved, before injection, in sterile sea water or normal saline solution, according as they were to be introduced into fresh or salt water animals. The mode of injection varied with the animal species employed: in higher forms the peritoneum was selected, in lower forms the body cavities or water vascular system. Some of the vermes gave unsatisfactory results in respect to the dosage because of the strong muscular contraction produced by the needle puncture and the presence of septa throughout the body. It was almost impossible to calculate the exact amount of venom introduced into these animals.

Each experiment was accompanied by at least two control animals maintained under precisely the same external conditions. In every case in which the cause of

* Researches upon the Venom of Rattlesnake, with an Investigation on the Anatomy and Physiology of the Organs concerned. Smithsonian Miscellaneous Collections, volume XII, Washington, 1861.

death was doubtful the experiment was repeated. In general, it may be stated that the animals used in the experiments stood the necessary handling and captivity without serious drawbacks. But in a few instances the degree of sensitiveness to these procedures was found to be very great. Thus, in the case of several kinds of small fish, *e. g.*, pollack, silver-side, pipe-fish, this sensitiveness was so great that they did not survive beyond 24 hours in captivity. Animals surviving the injections were, as a rule, killed at the end of the experiment and examined for local and general lesions.

The results of the study are given in tabulated form.

In reviewing the tables, one is impressed with the wide degree of susceptibility to snake venom exhibited by cold-blooded animals. On analyzing the effects produced, it becomes quickly evident that cobra venom exerts little if any local action, although it is the most toxic of all venoms employed. Crotalus venom, on the other hand, while exhibiting the least general toxicity, displays the greatest local action. Water moccasin venom occupies an intermediate position in this regard.

The chief local effect produced by rattlesnake and water moccasin venoms is the escape of red blood corpuscles from the vessel; only rarely is macroscopic necrosis of tissue visible. This production of hæmorrhage is, however, not restricted to the site of injection of the venom, but in some animals generalized hæmorrhages also take place. This latter effect was noticed chiefly in fishes, from which the blood may escape in such large quantity from the gills as to color the sea water. In other instances, hæmorrhages into the skin occur, and I have noticed during life, in the dog-fish poisoned by Crotalus venom, the occurrence of intracranial hæmorrhage. Only one species of fish—the puffer—was wholly insusceptible to the locally irritating principles of venom; it succumbed, however, to the general toxic effects of all the venoms.

It would appear as if the chief toxic effects of Crotalus and moccasin venoms are the outcome of their local action, and yet the general toxic constituents which they contain cannot be without marked action in some cases. These venoms may, therefore, cause death either through a destructive local action or through the operation of the neurotoxin upon the central nervous system.

In the case of cobra venom, the toxic action must be ascribed to neurotoxin. There the local effects are almost nil, while the respiratory disturbances are very apparent. The poisoned animals suffer from dyspnœa and from motor paralysis. Among fishes cobra venom causes rapid loss of equilibrium, so that the venomized animal swims with a rotary motion until it becomes too weak to struggle further. Crotalus and moccasin venoms cause a far less degree of disturbance of equilibration, while, on the other hand, their action at the beginning is likely to be irritative; the animal dashes about furiously without exhibiting evidence of a marked loss of balance.

Speaking generally, cobra venom is most toxic and Crotalus venom least toxic for cold-blooded animals. Moreover, this rule applies to the different classes as well as to the various species of animals employed.

In other words, cold-blooded animals are more highly susceptible to the toxic

action of neurotoxin than to that of hæmorrhagin.* Crotalus venom is effective chiefly in those instances in which the local lesions are marked; while in instances in which it acts independently of the local lesions a far larger dose, in keeping with its small proportional content of neurotoxin, is required to produce fatal results.

Snakes and frogs succumb easily to cobra venom, but they are relatively insusceptible to Crotalus and moccasin venoms. They would seem to be entirely resistant to the action of hæmorrhagin. Turtles are more susceptible to all venoms than the foregoing animals, and fishes exceed turtles in this respect. The grasshopper succumbs only to large doses of venom. Among the crustaceans the horseshoe crab is almost insusceptible, and other species of crabs are only moderately susceptible to venom poisoning. The lobster is only moderately resistant.

Excepting the earth-worm, all the worms with which I experimented showed a low degree of susceptibility. While the first will die *in toto* if injected with venom, the others show at times general effects, but they suffer only partial necrosis, from which they finally recover. After separation of the dead parts the worms seem to have been entirely restored. On the injection of Phascoloscoma with an enormous dose of venom I have seen the muscular contractibility of the injected part disappear for a period of a week or longer, but in the end it was recovered. If necrosis occurred a slough was formed and was finally cast off.

Upon the Echinodermata venoms produce little effect. The sea-urchin succumbed to all the venoms, while starfish and sea-cucumbers were not perceptibly affected.

The general toxicity of venoms upon the adult organism, as compared to their special effects which are produced upon the embryological elements† of the same species, is found to be of considerable interest. The ova or spermatozoa of some vermes and echinodermata are easily dissolved or fragmented by venoms, while the adults of corresponding species are proved to be almost entirely insusceptible to them.

On the other hand, the reverse is possible. Thus, the eggs of the Fundulus—a fish—are comparatively insusceptible to venoms, as they can be fertilized in the sea water containing rather a large amount of venoms and development of the fertilized ova progresses in the normal way, but the adults are found to be highly susceptible to the same kind of venoms.

A close examination as to the relation existing between the general toxicity and the hæmatoxic power‡ of venoms upon cold-blooded animals adds further interesting as well as important facts to the understanding of the nature of the action of snake venom *in vivo*.

In the following tables the letter *d* indicates that death followed the experiment.

---

* Flexner and Noguchi. The Constitution of Snake Venom and Snake Sera. Journal of Pathology and Bacteriology, 1903, VIII, 396.

† Flexner and Noguchi. On the Plurality of Cytolysins in Snake Venom. Univ. of Penna. Medical Bulletin, 1903, July–August.

‡ Noguchi. The Effects of Venom upon the Blood of Cold-Blooded Animals. Univ. of Penna. Medical Bulletin, 1903, July–August.

The Effects of Snake Venom Upon Cold-Blooded Vertebrates.

REPTILIA.

Animal.	Weight (grams).	Venom.	Dose.	Mode of injection.	General and local symptoms.	Result.
Cyclophis vernalis (Green snake)						
No. 1.	110	Cobra	2 mg.. .	Intraperitoneally.	Unable to crawl or coil after 6 hours; none locally. *Autopsy:* no hæmorrhage.	*d* 12 hours.
No. 2.	80	Moccasin ..	5 mg....	do.....	Rendered slightly inactive during first 12 hours; none locally.	Survived.
No. 3.	95	Crotalus....	5 mg....	do.....	Almost no symptoms	Survived.
Chelopus guttatus (Speckled turtle)						
No. 1.	400	Cobra	1 mg....	do.....	Paralytic action. *Autopsy:* slight local hæmorrhage along needle puncture.	*d* 2¼ hours.
No. 2.	300	Moccasin...	1 mg....	do.....	Caused stupor lasting 16 hours.....	Recovered.
No. 3.	350	Moccasin...	2 mg....	do.....	Paralytic symptoms; no local swelling. *Autopsy:* moderate hæmorrhage in peritoneum and viscera.	*d* 48 hours.
No. 4.	320	Crotalus....	5 mg....	do.....	Irritative action; none locally.....	Recovered.
No. 5.	300	Crotalus....	10 mg...	do.....	None locally; irritative action marked. *Autopsy:* marked hæmorrhage.	*d* 72 hours.
Chrysemys picta (Painted turtle)						
No. 1.	550	Cobra.....	1 mg....	do.....	Slightly inactive during first 12 hours, but became quite well after one day; none locally.	Recovered.
No. 2.	500	Cobra.....	2 mg....	do.....	Paralytic symptoms. *Autopsy:* only slight injection of vessels locally.	*d* 2 hours.
No. 3.	450	Moccasin...	1 mg	do..	Paralytic action, no local swelling. *Autopsy:* moderate hæmorrhage in peritoneum.	*d* 40 hours.
No. 4.	500	Crotalus....	1 mg....	do.....	Irritative action. *Autopsy:* moderate hæmorrhage.....	*d* 72 hours.
Chelydra serpentina (Snapping turtle)						
No. 1.	2000	Cobra	1 mg....	do.....	Temporary stupor lasting 12 hours; none locally	Recovered.
No. 2.	1900	Cobra	5 mg....	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 3 hours.
No. 3.	2500	Moccasin...	10 mg...	do.....	Paralytic action. *Autopsy:* moderate hæmorrhage	*d* 10 hours.
No. 4.	1800	Crotalus....	10 mg...	do.....	Irritative action for 30 minutes; animal then became gradually paralytic. *Autopsy:* moderate hæmorrhage.	*d* 96 hours.

AMPHIBIA.

Rana catesbiana (Bullfrog)						
No. 1.	95	Cobra	1 mg....	Intraperitoneally.	Slight temporary stupor; none locally	Recovered.
No. 2.	90	Cobra	5 mg....	do.....	Quickly paralyzed; none locally. *Autopsy:* no hæmorrhage.	*d* 3 hrs. 42 mins.
No. 3.	95	Moccasin ..	10 mg...	do..	Slight stupor for 2 hours; no local swelling	Recovered.
No. 4.	85	Moccasin ..	20 mg...	do.....	First irritative, then paralytic; no local action. *Autopsy:* no hæmorrhage.	*d* 12 hours.
No. 5.	90	Crotalus....	20 mg...	do.....	Almost no symptoms.....	Remained well over a week.
No. 6.	98	Crotalus....	40 mg...	do.....	Almost no symptoms; no hæmorrhage in peritoneum and viscera.	Killed for examination after 24 hours.

PISCES.

Acanthus sp.? (Sculpin)						
No. 1.	280	Cobra	1 mg....	Intraperitoneally.	Loss of equilibrium, paralysis of fins; no local action. *Autopsy:* no hæmorrhage.	*d* 30 minutes.
No. 2.	300	Moccasin ..	2 mg....	do..	Paralytic action. *Autopsy:* slight hæmorrhage.....	*d* 45 minutes.
No. 3.	290	Crotalus....	5 mg....	do.....	Irritative action; slight hæmorrhage around needle puncture.	Recovered.
No. 4.	310	Crotalus....	10 mg...	do.....	Strong irritation; hæmorrhagic spots near needle puncture. *Autopsy:* strong hæmorrhage.	*d* 12 hours.
Amphiuma means (Congo eel)						
No. 1.	5000	Cobra.....	5 mg....	do.....	Paralytic action; none locally.....	*d* 24 hours.
No. 2.	6000	Moccasin...	10 mg...	do..	First irritative action, then paralytic. *Autopsy:* marked hæmorrhage.	*d* 48 hours.
No. 3.	6500	Crotalus....	20 mg...	do.....	Strong irritation for first 30 minutes. After 36 hours local necrosis followed. *Autopsy:* moderate hæmorrhage in peritoneum, viscera, and the surrounding tissue; muscles around injection site partly necrotised.	*d* 48 hours.
Anguilla chrisypa (Sea eel)						
No. 1.	400	Cobra	1 mg....	do.....	Paralytic action. *Autopsy:* slight hæmorrhage.....	*d* 10 hours.
No. 2.	380	Moccasin ..	2 mg....	do.....	First irritative, then paralytic. *Autopsy:* slight hæmorrhage.	*d* 20 hours.
No. 3.	370	Crotalus....	2 mg....	do.....	Irritative action only.	Recovered.
No. 4.	380	Crotalus....	5 mg....	do.....	Strong irritation. *Autopsy:* marked hæmorrhage.....	*d* 40 hours.

The Effects of Snake Venom Upon Cold-Blooded Vertebrates—Continued.

PISCES—Continued.

Animal.	Weight (grams).	Venom.	Dose.	Mode of injection.	General and local symptoms.	Result.
Apeltes quadracus (Stickleback)						
No. 1.	2	Cobra	0.1 mg.	Intraperitoneally.	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 12 minutes.
No. 2.	2.5	Moccasin ..	0.1 mg	do.....	Irritative action. *Autopsy:* slight hæmorrhage.....	*d* 30 minutes.
No. 3.	2.2	Crotalus....	0.1 mg.	do.....	Irritative action. *Autopsy:* slight hæmorrhage..	*d* 1 hr. 15 mins.
Brevoortia tyrannus (Menhaden)						
No. 1.	400	Cobra	1 mg....	do.....	Paralytic action. *Autopsy:* slight hæmorrhage.....	*d* 1 hr. 10 mins.
No. 2.	360	Moccasin ..	1 mg....	do.... ...	Irritative action; blood escaped from gills. *Autopsy:* marked hæmorrhage.	*d* 2 hrs. 10 mins.
No. 3.	400	Moccasin ..	5 mg....	do.....	Irritative action; blood escaped from gills. *Autopsy:* very marked hæmorrhage.	*d* 30 minutes.
No. 4.	380	Crotalus....	1 mg....	do.....	Irritative action; ecchymotic spots over body. *Autopsy:* necrosis around needle puncture; marked hæmorrhage in peritoneum and viscera.	*d* 16 hours.
No. 5.	400	Crotalus....	5 mg....	do..	Irritative action; blood escaped from gills. *Autopsy:* marked hæmorrhage.	*d* 5 hours.
Clupea harengus (Herring)						
No. 1.	450	Cobra	1 mg....	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 15 minutes.
No. 2.	400	Moccasin ..	1 mg....	do.....	Irritative, then paralytic action. *Autopsy:* moderate hæmorrhage.	*d* 1 hr. 15 mins.
No. 3.	420	Crotalus....	1 mg....	do.....	Irritative action; blood escaped from gills; numerous ecchymotic spots over injected side of body. *Autopsy:* very marked hæmorrhage and softening of muscles around needle puncture.	*d* 4 hours.
Cynoscion regalis (Squeteague)						
No. 1.	1200	Cobra	1 mg....	do.....	Paralytic action; none locally. *Autopsy:* slight hæmorrhage.	*d* 1 hr. 25 mins.
No. 2.	1500	Moccasin ..	1 mg....	do.....	Irritative action; convulsions. *Autopsy:* moderate hæmorrhage.	*d* 3 hours.
No. 3.	1000	Crotalus....	2 mg....	do.....	Irritative action; convulsions. *Autopsy:* very marked hæmorrhage.	*d* 5 hours.

Fundulus heteroclitus (Minnow)						
No. 1.	30	Cobra	1 mg....	do.....	Paralytic action; none locally. *Autopsy:* no hæmorrhage.	*d* 2 hrs. 5 mins.
No. 2.	35	Cobra	2 mg....	do.....	Rapid paralysis. *Autopsy:* slight hæmorrhage.....	*d* 45 minutes.
No. 3.	32	Moccasin ..	2 mg....	do.....	Irritative action. *Autopsy:* moderate hæmorrhage	*d* 1 hr. 40 mins.
No. 4.	34	Crotalus....	5 mg....	do..	Irritative action. *Autopsy:* very marked hæmorrhage....	*d* 3 hrs. 15 mins.
Microgadus tomcod (Tom-cod)						
No. 1.	90	Cobra	1 mg....	do.....	Paralytic action. *Autopsy:* slight hæmorrhage.....	*d* 45 minutes.
No. 2.	70	Moccasin ..	1 mg...	do..	Paralytic action. *Autopsy:* slight hæmorrhage.....	*d* 30 minutes.
No. 3.	85	Crotalus..	2 mg....	do.....	Irritative action; convulsions. *Autopsy:* moderate hæmorrhage.	*d* 5 hours.
Morone americana (White perch)						
No. 1.	100	Cobra	1 mg....	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 2 hrs. 20 mins.
No. 2.	110	Moccasin ..	1 mg....	do.....	Irritative action. *Autopsy:* marked hæmorrhage.....	*d* 4 hrs. 50 mins.
No. 3.	150	Crotalus....	5 mg....	do..	Marked irritative action. *Autopsy:* marked hæmorrhage.	*d* 6 hrs. 55 mins.
Poronotus triacanthus (Butter-fish)						
No. 1.	420	Cobra	1 mg. .	do.....	Paralytic action, none locally. *Autopsy:* no hæmorrhage.	*d* 40 minutes.
No. 2.	400	Moccasin ..	1 mg....	do.....	Irritative action absent. *Autopsy:* moderate hæmorrhage.	*d* 1 hour.
No. 3.	450	Crotalus....	1 mg....	do.....	Irritative action absent. *Autopsy:* slight hæmorrhage...	*d* 4 hours.
Mustelus canis (Smooth dog-fish)						
No. 1.	600	Cobra	2 mg....	do.....	Paralytic action; none locally. *Autopsy:* no hæmorrhage.	*d* 1 hr. 30 mins.
No. 2.	550	Moccasin ..	2 mg....	do.....	Irritative action; many ecchymotic spots over body and hæmorrhage in cranial cavity visible. *Autopsy:* marked hæmorrhage in peritoneum, viscera, and in cranial cavity.	*d* 16 hours.
No. 3.	500	Crotalus....	2 mg...	do.....	Irritative action; many ecchymotic spots over body; hæmorrhage visible in cranial cavity. *Autopsy:* very marked hæmorrhage in peritoneum, viscera, cranium.	*d* 20 hours.
Menidia notata (Silverside)						
No. 1.	13	Cobra	0.1 mg.	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 25 minutes.
No. 2.	12	Moccasin ..	0.5 mg.	do.....	Highly irritative action. *Autopsy:* slight hæmorrhage ...	*d* 20 minutes.
No. 3.	14	Crotalus....	0.5 mg.	do.....	Highly irritative action; convulsions. *Autopsy:* slight hæmorrhage.	*d* 1 hour.
Mugil cephalus (Jumping mullet)						
No. 1.	5	Cobra	0.1 mg.	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 35 minutes.
No. 2.	4.5	Moccasin ..	0.5 mg.	do.....	Irritative action. *Autopsy:* moderate hæmorrhage.....	*d* 30 minutes.
No. 3.	4	Crotalus....	0.5 mg.	do.....	Irritative action. *Autopsy:* moderate hæmorrhage...	*d* 1 hr. 30 mins.

The Effects of Snake Venom Upon Cold-Blooded Vertebrates—Continued.

PISCES—Continued.

Animal.	Weight (grams).	Venom.	Dose.	Mode of injection.	General and local symptoms.	Result.
Opsanus tau (Toad fish)						
No. 1.	500	Cobra	2 mg....	Intraperitoneally.	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 3 hours.
No. 2.	550	Moccasin ..	2 mg....	do.....	Irritative action. *Autopsy:* slight hæmorrhage.....	*d* 16 hours.
No. 3.	480	Crotalus...	2 mg....	do.....	Highly irritative action; none locally. *Autopsy:* no hæmorrhage.	*d* 7 hours.
Osmerus mordax (Smelt)						
No. 1.	25	Cobra	0.5 mg..	do.....	Paralytic action; none locally. *Autopsy:* no hæmorrhage.	*d* 15 minutes.
No. 2.	30	Moccasin ..	1 mg....	do.....	Irritative action. *Autopsy:* moderate hæmorrhage.....	*d* 20 minutes.
No. 3.	27	Crotalus....	1 mg...	do.....	Irritative action. *Autopsy:* moderate hæmorrhage.....	*d* 40 minutes.
Paralichthys dentatus (Summer flounder)						
No. 1.	1000	Cobra	2 mg....	do.....	Paralytic action; none locally. *Autopsy:* slight hæmorrhage.	*d* 2 hrs. 10 mins.
No. 2.	1200	Moccasin ..	5 mg....	do.....	Irritative action followed by later paralytic effect. *Autopsy:* moderate hæmorrhage.	*d* 6 hours.
No. 3.	800	Crotalus....	5 mg....	do.....	Irritative action; local swelling. *Autopsy:* marked hæmorrhage.	*d* 96 hours.
Pseudopleuronectes americanus (Flat fish)						
No. 1.	200	Cobra	1 mg....	do.....	Paralytic action; none locally. *Autopsy:* no hæmorrhage.	*d* 12 hours.
No. 2.	250	Moccasin ..	2 mg....	do.....	Irritative action. *Autopsy:* marked hæmorrhage.....	*d* 15 hours.
No. 3.	220	Crotalus....	2 mg....	do.....	Irritative action. *Autopsy:* marked hæmorrhage.....	*d* 25 hours.
Prionotus strigatus (Red sea-robin)						
No. 1.	400	Cobra	2 mg ...	do..	Paralytic action. *Autopsy:* no hæmorrhage.	*d* 4 hours.
No. 2.	510	Moccasin ..	2 mg....	do.....	Irritative action; later paralytic effect. *Autopsy:* marked hæmorrhage.	*d* 6 hours.
No. 3.	390	Crotalus....	5 mg....	do..	Highly irritative action; blood escaped from gills. *Autopsy:* very marked hæmorrhage.	*d* 10 hours.

Raja sp. (Summer skate)						
No. 1.	800	Cobra	2 mg. ..	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 1 hr. 50 mins.
No. 2.	750	Moccasin ..	5 mg....	do.....	Irritative action. *Autopsy:* moderate hæmorrhage.....	*d* 2 hours.
No. 3.	500	Crotalus....	10 mg...	do.....	Irritative action. *Autopsy:* marked hæmorrhage.....	*d* 6 hours.
Carcharinus littoralis (Sand shark)						
No. 1.	12000	Cobra	5 mg....	do..	Paralytic action; none locally. *Autopsy:* no hæmorrhage.	*d* 24 hours.
No. 2.	15000	Moccasin ..	20 mg...	do.....	Irritative action; local necrosis under skin around needle puncture. *Autopsy:* marked hæmorrhage.	*d* 40 hours.
No. 3.	13500	Moccasin ..	10 mg...	do.....	Irritative action; local softening after 30 hours. In course of a week it is completely cured.	Recovered.
No. 4.	13000	Crotalus....	20 mg...	do.....	Irritative action. *Autopsy:* moderate hæmorrhage.....	*d* 96 hours.
Raja ocellata (Winter skate)						
No. 1.	3000	Cobra	2 mg....	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 2 hours.
No. 2.	3500	Moccasin ..	5 mg....	do.....	Irritative action, then paralytic. *Autopsy:* slight hæmorrhage.	*d* 2 hrs. 20 mins.
No. 3.	2800	Crotalus....	10 mg...	do.....	Irritative action, then paralytic. *Autopsy:* slight hæmorrhage.	*d* 10 hours.
Raja lævis (Barn-door skate)						
No. 1.	9200	Cobra	5 mg....	do.....	Paralytic action; none locally.....	*d* 12 hours.
No. 2.	8000	Cobra	2 mg....	do.....	Inactive for 24 hours, but recovered after 48 hours.....	Recovered.
No. 3.	10000	Moccasin ..	20 mg...	do.....	Irritative action. *Autopsy:* moderate hæmorrhage.....	*d* 7 hours.
No. 4.	9500	Crotalus....	20 mg .	do..	Irritative action. *Autopsy:* moderate hæmorrhage.....	*d* 24 hours.
Siphostoma fuscum (Pipe-fish)						
No. 1.	6	Cobra	0.1 mg.	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 10 minutes.
No. 2.	5	Moccasin ..	0.1 mg.	do.....	Irritative action. *Autopsy:* slight hæmorrhage.....	*d* 30 minutes.
No. 3.	5	Crotalus....	0.1 mg.	do.....	Irritative action. *Autopsy:* slight hæmorrhage.....	*d* 35 minutes.
Spheroides maculatus (Puffer)						
No. 1.	200	Cobra	1 mg....	do.....	Inactive for some hours.....	Recovered.
No. 2.	210	Cobra	4 mg....	do..	Paralytic action. *Autopsy:* no hæmorrhage.	*d* 1 hr. 5 mins.
No. 3.	150	Moccasin ..	4 mg....	do.....	Irritative action. *Autopsy:* no hæmorrhage.....	*d* $2\frac{1}{4}$ hours.
No. 4.	180	Crotalus....	4 mg....	do.....	Irritative action. *Autopsy:* no hæmorrhage.....	*d* 8 hours.
Stenotomus chrysops (Scup)						
No. 1.	400	Cobra	1 mg...	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 4 hours.
No. 2.	420	Moccasin ..	1 mg....	do.....	Irritative action. *Autopsy:* marked hæmorrhage.....	*d* 10 hours.
No. 3.	380	Crotalus....	1 mg....	do.....	Irritative action. *Autopsy:* very marked hæmorrhage ...	*d* 15 hours.

The Effects of Snake Venom Upon Cold-Blooded Vertebrates—Continued.

PISCES—Continued.

Animal.	Weight (grams).	Venom.	Dose.	Mode of injection.	General and local symptoms.	Result.
Tautogolabrus adspersus (Cunner)						
No. 1.	50	Cobra	1 mg....	Intraperitoneally.	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 56 minutes.
No. 2.	50	Moccasin ..	1 mg....	do.....	Irritative action; marked hæmorrhage from the gills. *Autopsy:* very marked hæmorrhage.	*d* 6 hours.
No. 3.	45	Moccasin ..	5 mg....	do.....	Hæmorrhage from gills lasting to the death. *Autopsy:* anæmic condition of the internal organs; local hæmorrhage very marked.	*d* 1 hour.
No. 4.	40	Crotalus....	1 mg....	do.....	Hæmorrhage from gills. *Autopsy:* marked anæmia of all organs; hæmorrhage into peritoneal cavity.	*d* 5 hours.
No. 5.	50	Crotalus....	5 mg....	do.....	Hæmorrhage from gills. *Autopsy:* anæmia and hæmorrhage of all organs.	*d* 2½ hours.
Tautoga onitis (Tautog)						
No. 1.	200	Cobra	1 mg....	do.....	Paralytic action. *Autopsy:* no hæmorrhage.....	*d* 3 hours.
No. 2.	250	Moccasin ..	2 mg....	do.....	Irritative action; local necrosis after 10 hours. *Autopsy:* moderate hæmorrhage.	*d* 15 hours.
No. 3.	180	Crotalus....	2 mg..	do.....	Irritative action, later paralytic. *Autopsy:* slight hæmorrhage.	*d* 7 hours.
Centropristes striatus (Sea bass)						
No. 1.	500	Cobra	2 mg. ..	do..	Paralytic action. *Autopsy:* slight hæmorrhage.....	*d* 2 hours.
No. 2.	480	Moccasin ..	2 mg....	do.....	Irritative action. *Autopsy:* moderate hæmorrhage and extensive local necrosis.	*d* 4¾ hours.
No. 3.	580	Crotalus....	2 mg. .	do.....	Irritative action. *Autopsy:* marked hæmorrhage and extensive local necrosis.	*d* 12 hours.

INSECTA.

Animal.	Weight (grams).	Venom.	Dose.	Mode of injection.	General and local symptoms.	Result.
Acridium americanus (Grasshopper)						
No. 1.	4	Cobra.....	1 mg...	Intraperitoneally.	Paralytic action.....	*d* 30 minutes.
No. 2.	3.5	Moccasin..	1 mg....	do.....	After 10 hours unable to jump, still later unable to hold its body and fell to bottom of cage.	*d* 16 hours.
No. 3.	3.8	Crotalus....	1 mg....	do.....	Irritative action at first, then became gradually weaker....	*d* 24 hours.

CRUSTACEA.

Carcinus granulatus (Green crab)						
No. 1.	30	Cobra.....	1 mg..	Intracrustaceally.	Paralytic action.....	*d* 35 minutes.
No. 2.	35	Moccasin..	1 mg...	do.....	Irritative action, later paralytic.....	*d* 1 hr. 35 mins.
No. 3.	32	Crotalus...	1 mg....	do.....	Highly irritative action.....	*d* 3 hrs. 15 mins.
Eupagurus pollicaris (Large hermit crab)						
No. 1.	25	Cobra.....	1 mg...	do.....	Paralytic action.....	*d* 15 minutes.
No. 2.	20	Moccasin..	2 mg...	do.....	Irritative, then paralytic action.....	*d* 3 hours.
No. 3.	22	Crotalus....	2 mg....	do.....	Highly irritative action.....	*d* 2 hrs. 45 mins.
Homarus americanus (Lobster)						
No. 1.	300	Cobra.....	2 mg....	do.....	Paralytic action.....	*d* 2 hours.
No. 2.	320	Cobra.....	5 mg...	do.....	Paralytic action only.....	*d* 15 minutes.
No. 3.	350	Moccasin..	10 mg...	do.....	Paralytic action.....	*d* 15 minutes.
No. 4.	300	Moccasin..	5 mg...	do.....	Paralytic action.....	*d* 2 hrs. 50 mins.
No. 5.	300	Crotalus....	10 mg.	do.....	Irritative, then paralytic action.....	*d* 35 minutes.
No. 6.	350	Crotalus....	5 mg....	do.....	Irritative action.....	*d* 4 hrs. 35 mins.
Libinia canaliculata (Spider crab)						
No. 1.	40	Cobra.....	2 mg....	do.....	Paralytic action.....	*d* 10 minutes.
No. 2.	30	Moccasin..	2 mg....	do.....	Paralytic action.....	*d* 35 minutes.
No. 3.	35	Crotalus....	2 mg....	do.....	Paralytic action; slight irritation for first few minutes.....	*d* 2 hrs. 10 mins.

The Effects of Snake Venom Upon Invertebrates—Continued.

CRUSTACEA—Continued.

Animal.	Weight (grams).	Venom.	Dose.	Mode of injection.	General and local symptoms.	Result.
Limulus polyphemus (Horseshoe crab)						
No. 1.	700	Cobra	1 mg....	Intracrustaceally.	Slightly stupid for first hour, but quickly recovered..	Recovered.
No. 2.	850	Cobra	10 mg...	do.	Slightly stupid for some hours, but after 12 hours quite active again.	Recovered.
No. 3.	920	Cobra	20 mg...	do.....	Paralytic action.....	*d* 6 hours.
No. 4.	900	Moccasin ..	1 mg....	do.....	Irritative action lasting about 15 minutes	Survived.
No. 5.	1000	Moccasin ..	5 mg....	do.....	Temporary irritation.....	Survived.
No. 6.	950	Moccasin ..	10 mg...	do.....	Temporary irritation, then paralytic action.....	*d* 40 hours.
No. 7.	1100	Crotalus....	10 mg...	do.....	Irritative action.....	*d* 16 hours.
Platyonichus ocellata (Lady crab)						
No. 1.	38	Cobra	1 mg....	do.....	Paralytic action.....	*d* 35 minutes.
No. 2.	40	Moccasin ..	2 mg....	do.....	Irritative action, then paralytic action.....	*d* 2 hrs. 18 mins.
No. 3.	36	Crotalus....	2 mg....	do.....	Highly irritative action.....	*d* 6 hrs. 30 mins.
VERMES.						
Lumbricus terrestris (Earth worm)						
No. 1.	10	Cobra	*5 mg...	Body cavity	Needle puncture caused very strong muscular contraction of whole body, and fluid escaped from hole as soon as needle was drawn off. Exact amount of venom which remained in body is not to be calculated out. It produced slight inactivity of the worm for 1 hour, but afterwards showed no further symptoms; 3 hours later animal is again active.	Survived.
No. 2.	11.5	Cobra	†20 mg.	do.....	Strong contraction of body offered same difficulty to introduce the venom solution in satisfactory manner, but the greater part of fluid remained in body cavity. The muscular contractibility became gradually weaker, and after 12 hours it completely disappeared. During this time necrosis of injected part developed.	*d* 12 hours.
No. 3.	9	Moccasin ..	†20 mg.	do.....	Reflex action disappeared after 20 hours. Œdema and necrosis of injected part.	*d* 20 hours.
No. 4.	9.5	Crotalus....	†20 mg.	do.....	Reflex action disappeared after 18 hours. Œdema and necrosis of injected part.	*d* 18 hours.

*(In 0.5 c. c.)

†(In 0.2 c. c.)

Phascoloscoma gouldii						
No. 1.	7	Cobra.....	†10 mg.	do.....	As strong muscular contraction resulted from needle puncture only an unsatisfactory injection was possible. The muscular contractibility of injected part became gradually weaker, and it has disappeared after 36 hours; this paralyzed part became finally necrotised. On the other hand, the rest of body suffered no inconvenience although it had an enormous œdema along whole length. Œdema disappeared after two weeks.	Necrosis of injected part, and œdema of whole body. Recovered after 2 weeks.
No. 2.	5.5	Moccasin..	†10 mg.	do.....	Similar effects to those caused by cobra venom, except œdema was stronger and persisted over two weeks.	Necrosis of injected part, and œdema of whole body. Recovery did not take place even after 2 weeks.
No. 3.	5	Crotalus....	†10 mg.	do.....	Instead of producing general œdema it caused numerous small vesicles over whole body, otherwise quite similar effects of above-named venoms.	Idem.
Nereis virens (Clam worm)						
No. 1.	12	Cobra.....	†10 mg.	do.....	Separated into two ends from injection site, otherwise no effects.	Both pieces quite active for many days
No. 2.	15	Moccasin..	†20 mg.	do.....	Do.	
No. 3.	13	Crotalus....	†20 mg.	do.....	Do.	
			MOLLUSCA.			
Loligo pealii						
No. 1.	170	Cobra.....	10 mg...	Intravascularly.	Paralytic action.....	*d* 1 hr. 12 mins.
No. 2.	150	Moccasin..	10 mg...	do.....	Irritative action, then paralytic action.....	*d* 1½ hours.
No. 3.	160	Crotalus....	10 mg...	do.....	Idem.....	*d* 2 hours.

† (In 0.2 c. c.)

The Effects of Snake Venom Upon Invertebrates—Continued.

ECHINODERMATA.

Animal.	Weight (grams).	Venom.	Dose.	Mode of injection.	General and local symptoms.	Result.
Asterias vulgaris (Star-fish)						
No. 1.	30	Cobra.....	10 mg...	Arm.....	Slight stupefaction lasting 1 hour.....	Survived.
No. 2.	25	Moccasin..	10 mg...	do.....	No effects. No symptoms developed within 4 weeks.	
No. 3.	32	Crotalus....	10 mg...	do..	Do.	
Arbacia punctulata (Purple sea-urchin)						
No. 1.	30	Cobra.	5 mg....	Body cavity	Movement of pedicules gradually ceased. Spines not easily breakable.	*d* 20 hours.
No. 2.	29	Moccasin..	5 mg....	do.....	Similar effects as cobra venom, but spines came off easily by slight pressure.	*d* 25 hours.
No. 3.	31	Crotalus....	5 mg....	do.....	Similar effects as moccasin venom.....	*d* 48 hours.
Pentacta frondosa (Northern sea-cucumber)						
No. 1.	35	Cobra.....	20 mg ..	do.....	No effects. No symptoms developed within 4 weeks.	
No. 2.	31	Moccasin..	20 mg...	do.....	Do.	
No. 3.	42	Crotalus....	20 mg	do.....	Do.	